

REMARKS

Status of the Claims

Claims 1-40 are in the application.

Claims 1-40 were rejected.

By way of this amendment claims 1, 34 and 40 have been amended.

Upon entry of this amendment, claims 1-40 will be pending.

Drawings

Applicant respectfully disagrees that the drawing should be objected to but is attempting to obtain a higher quality copy to advance the application. Such replacement sheet shall be provided in a separate reply.

Summary of the Amendment

Claim 1 has been amended to more clearly set forth the subject matter of the invention. As amended, section (f) has been rewritten to more clearly set forth that the 3' end of one strand of a double stranded DNA molecule is coupled to the 5' end of the other strand of the same double stranded DNA molecule. As amended, the claim clearly sets forth that the two separate strands of the double stranded DNA molecule are formerly two separate DNA molecules hybridized to each other which are coupled to form a single DNA molecule that is hybridized to itself. In addition, claim 1 has been amended to remove language that lacked antecedent bases.

Claim 34 has been amended to remove language that lacked antecedent bases.

Claim 40 has been amended to refer to the subsections of claim 1 with the proper subsection designation.

Support for the amendments is found throughout the specification. No new matter has been added.

Claim Rejections – 35 U.S.C. § 112

Claims 1-40 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particular point out and distinctly claim the subject matter which applicant regards as the invention. It is asserted that (a) the claims are confusing and (b) language in the claims lacks antecedent basis.

The claims have been amended to address the clarity and antecedent basis issues raised in the Official Action.

(a) It is asserted that claims 1-40 are confusing. It is asserted that steps (f) through (h) of claim 1 are unclear regarding how the coupling step operates to identify the alternatively spliced RNA. The Office noted that for example it is unclear if the coupling step (f) is intended to encompass ligation between the two strand ends of every cross-hybridized double stranded cDNA from step (e) such that loops are formed or if the strands of each of the selected cross hybridized double stranded cDNAs from step (e) are coupled to each other or something entirely different. Additionally the coupling step is confusing in the last two lines of step (f) because if double stranded DNA is denatured (even after being coupled or ligated) it would be obvious that single stranded molecules would be formed.

Step (f) of claim 1 has been amended to recite:

coupling at one end of the 3' end of one strand of a cross-hybridized double-stranded cDNA molecule selected in step (e) to the 5' end of the other strand of said cross-hybridized double-stranded cDNA molecule to form a loop and produce a coupled cross-hybridized double-stranded cDNA molecule that comprises at least one area of mismatched sequence, wherein when denatured said coupled cross-hybridized double-stranded cDNA molecule is a single linear single stranded nucleic acid molecule;

As amended, step (f) clearly states that the 3' end of one strand of a cross-hybridized double-stranded cDNA molecule selected in step (e) is coupled to the 5' end of the **other strand of the same cross-hybridized double-stranded cDNA molecule**. This coupling of the two strands of the same double stranded cDNA molecule at the 3' end of one strand and the 5' end of the other strand forms a loop in which the two ends are connected. The coupled strands are linked at one end and when denatured the strands are each a part of the same single linear single stranded molecule.

As amended, the claim clearly sets forth that cross hybridized double-stranded cDNA molecule which contain mismatches are formed by combining, denaturing and annealing cDNA molecules from a first cDNA populations labeled with a selectable tag and a second cDNA populations labeled with a different selectable tag (step (c)). The cross hybridized double-stranded cDNA molecules can be isolated because they contain both selectable tags (step d)). Cross hybridized double-stranded cDNA molecules which contain a sequence mismatch are then isolated (step (e)). These cross hybridized double-stranded cDNA molecules which contain a sequence mismatch are then coupled so that a single double-stranded cDNA molecule made up of two single stranded molecules are linked to each other (step (f)) such that when denatured the double-stranded cDNA molecules to form a single linear single stranded DNA molecule (step (g)). Analysis of the sequence of a single linear single stranded DNA molecule is used to identify the sequence of an alternatively spliced RNA (step (h)).

As amended, claim 1 and dependent claims 2-40 are clear and definite. As amended, it is clear how the coupling step operates to identify the alternatively spliced RNA. The coupling step (f) clearly sets forth the ligation of the 3' end of one strand of a cross-hybridized double stranded cDNA molecule to the 5' end of the other strand of the same cross-hybridized double stranded cDNA molecule. It is clear as amended that denaturing of the coupled double stranded DNA molecule produces a **single** linear single stranded DNA molecule. The formation of a **single** linear single stranded DNA molecule from the denaturation of a double stranded DNA molecule necessarily requires that the two strands are linked to each by means in addition to the hybridization of complementary sequences. As amended, the claims are clear and definite.

(b) It is asserted that claims 1-40 lack antecedent basis for the phrase "region of the sequences". Claims 1 and 34 have been amended to remove the unclear language. The claims accordingly in compliance with the requirements of the second paragraph of 35 U.S.C. 112.

As amended, claims 1-40 are clear and definite, and particular point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully requests that the rejection of claims 1-40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particular point out and distinctly claim the subject matter which applicant regards as the invention, be withdrawn/

Conclusion

Claims 1-40 are in condition for allowance. Applicant respectfully requests that the amendment be entered and the application proceed to allowance. Applicants invite the Examiner to contact the undersigned at 610.640.7855 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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